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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,418	10/07/2003	H. Michael Shepard	NB 2008.01 (060925-0801)	7416

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
10/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,418	SHEPARD ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 9, 2007 (amdt)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63,64,68-70,79,80,83,85-90 and 94-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *87-90* is/are allowed.

6)☒ Claim(s) *63,64,68-70,79,80,83,85,86 and 94-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/09/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims **1-62, 65-67, 71-78, 81-82, 84 and 91-93** have been cancelled, claims **63, 68-70, 79-80 and 87** have been amended, the disclosure has not been further amended, and new claims **94-99** have been added as per the amendment filed August 9, 2007. One additional or supplemental Information Disclosure Statement (1 IDS) has been filed on August 9, 2007 with a single additional prior art document.

Claims **63-64, 68-70, 79-80, 83, 85-90 and 94-99** remain in the case.

Examiner Note: Applicant at page 9 of the instant response, applicant has listed claims **63-64, 69-70, 79-80, 83, 85-90 and 94-99** as remaining under examination. Examiner will also be responding to claim **68** which appears to also remain under examination.

The disclosure is objected to because of the following informalities:

At page 55, line 26, the term "idodide" is a misspelling is
-- iodide --.

Appropriate correction is required.

Claims **63-64, 68-70, 79-80, 83, 85-86 and 94-99** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims extends to isomeric compounds the synthesis of which has not been defined in a manner permitting one of ordinary skill to know the identity of the compounds which have shown activity in the treatment of neoplastic disease conditions. In particular, claim **63** identifies compounds the synthesis and biological testing of which has <u>not</u> been disclosed, including
i) "wherein the compound may be in any enantiomeric, diastereoisomeric or stereoisomeric

form, including ... L-form, α-anomeric form." Only D-forms are disclosed as having been synthesized and as having the desired medicinal activity, and
ii) because there is no showing of either how to use the compounds defined by claim **83** or how to make or use examples across the entire range of alternative isomers listed in claim **63**. In addition, applicant has not supplied any data to support the extension of treatments to include "liver cancer."

B. The nature of the invention is directed to 5-substituted-2'-deoxyuridines and analogues thereof as defined by claim **63**, pharmaceutical compositions thereof, a method of testing for relative antineoplastic activity, and method of treating several different neoplastic disease conditions.

C. The state of the prior art is well established by the extensive lists of prior art patents and other references disclosed by the patents issued to Shepard and Shepard et al. listed on the instant PTO-892.

D. The level of one or ordinary skill is high because the practice of the invention requires knowledge of both the organic synthesis of nucleoside analogues and the medical knowledge and training required to properly administer and monitor antineoplastic agents to a host in need thereof.

E. The level of predictability in the art is limited because the number of compounds actually synthesized and/or tested, and the specific disease conditions tested, is very small when compared with the number of compounds included within the scope of the instant claims. In view of the lack complete test data, it is also unclear that the substitution of "Cl," or "I" for "Br" as an X-substituent will produce equivalent biological testing results. Similarly, most of the variations provided for by the alternatives within the definitions of variables R^6 and R^7 have neither been synthesized nor tested for biological activity. And, only three neoplastic cell types have been shown to be effectively inhibited. For this reason examiner concludes that the asserted and claimed extrapolation to the effective treatment of all listed "pathological" cell types found in claims **94 and 96** which overexpress thymidylate synthase is not sufficiently predictable and therefore not adequately enabled.

F. The amount of direction provided by the inventor is difficult to determine because of incomplete synthetic information and incomplete identifying information concerning the

identity of compounds tested for biological activity at pages 68-69. Applicant has not provided enabling support for the synthesis of "any enantiomeric, diastereomeric or stereoisomeric form," and in particular has not shown how to make the L-forms and the α-anomers of any of the claimed compounds, or shown that the asserted and claimed pharmaceutical activity or testing for said activity of claims **94-99** extends to all possible enantiomers and diastereomers and other than ß-D-isomers of some of the compounds defined by claim **63**.

G. The existence of working examples is difficult to determine because of incomplete identifying information concerning either the synthesis of many of the compounds claimed or the identity of compounds tested for biological activity at pages 68-70.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive in light of the very limited amount of biological test results and synthetic instructions provided for the compounds defined by claim **63**. In particular, the instant method of treatment claims are only enabled for the treatment of one variety of breast cancer, one variety of colon carcinoma, and one fibrosarcoma (HT 1080; organ apparently not specified in the disclosure) according to the table at page 70). Therefore, examiner concludes that the amount of experimentation required to practice all aspects of the instant claimed invention is undue in view of the lack of adequate quantities of relevant synthetic data and medicinally relevant test data in the disclosure.

Applicant's arguments filed August 9,2007 have been fully considered but they are not persuasive.

Examiner notes applicant's comments concerning the interview of June 12, 2007. In the last paragraph, applicant states that amendments were offered, but that " ... Examiner did not opine [on] the acceptability of these offered claim amendments to remove the outstanding rejections." Examiner recalls the interview somewhat differently, and did not agree to any amendments because the proposals offered seemed to be only a partial response to the complex of issues discussed, and because, in view of the complexity of the instant case, felt at the time that a re-review of a complete response officially submitted by applicant was the wisest course under the circumstances.

In re applicant's comments concerning the rejection under 35 U.S.C. §112, first paragraph, examiner has amended the above rejection to delete the method of testing claims **87-90** and to otherwise amend the rejection in view of the instant amendment and response.

Citing **Libra et al.** (PTO-1449 ref. **AR5**). applicant argues that, in view of the disclosure by **Libra et al.** that liver cancers sometimes include overexpression of thymidylate synthase (TS), that applicant should be permitted to assert that extrapolation of the instant claimed method of treatment to include liver cancers wherein TS is overexpressed, in spite of the lack of direct evidence that any one of the instant claimed active ingredients are effective in the treatment of any variety of liver cancer, including those caused by what **Libra et al.** asserts are metastases of a colorectal cancer. Examiner is not convinced, and previously cited *Ex parte Balzarini* because that case, along with other cases cited in the MPEP, establishes that the USPTO has the authority to ask for, and insist on, medicinal test data to establish that a claimed method of treatment of a disease in an unpredictable art area may be effectively treated by the claimed method.

In re the issue of isomers, applicant argues that the test data at page 70 of the disclosure involves mixtures of "isomers," thereby implying that the breadth of claim **63** is appropriate because more than one "isomer" has shown medicinally relevant activity. The isomers shown to have activity are geometric isomers at the unsaturated uridylate side chain, and are not the enantiomers, diastereomers or [alpha]-anomers listed in claim **63**.

Examiner concludes that applicant's arguments together with applicant's amendments have advanced prosecution, but have not entirely addressed all of the issues under 35 U.S.C. §112, first paragraph. For this reason the instant rejection has been maintained.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **63-64, 68-70, 79-80, 83, 85-86 and 94-99** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-10*** of U.S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Applicant's arguments filed July 24, 2006 have been fully considered but they are not deemed to be persuasive.

Applicant's arguments filed August 9, 2005 have deferred responding to the instant grounds of rejection pending a finding of allowable subject matter. No further comment on this rejection has been included within the instant response. Therefore, the instant rejection has been maintained.

Claims **87-90** are allowable as presently in the case.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no

event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

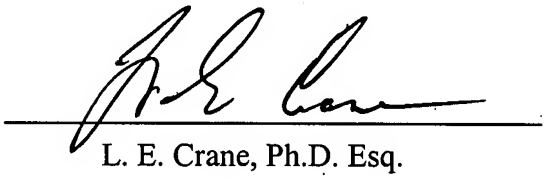
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. Telephone number for filing documents officially by FAX with the USPTO is **571-273-8300**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
10/19/2007



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